Disease and Injury Among Participants in the Agricultural Health Study

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Abstract. *The Agricultural Health Study (www.aghealth.org) is a cohort of 89,658 pesticide applicators and their spouses from Iowa and North Carolina assembled between 1993 and 1997 to evaluate risk factors for disease in rural farm populations. This prospective study is just now reaching sufficient maturity for analysis of many disease endpoints. Nonetheless, several analyses have already provided interesting and important leads regarding disease patterns in agricultural populations and etiologic clues for the general population. Compared to the mortality experience of the general population in the two states (adjusted for race, gender, age and calendar time), the cohort experienced a very low mortality rate overall and for many specific causes and a low rate of overall cancer incidence. A few cancers, however, appear elevated, including multiple myeloma and cancers of the lip, gallbladder, ovary, prostate, and thyroid, but numbers are small for many cancers. A study of prostate cancer found associations with exposure to several pesticides, particularly among individuals with a family history of prostate cancer. Links to pesticides and other agricultural factors have been found for injuries, retinal degeneration, and respiratory wheeze. Methodological studies have determined that information collected by interview is unbiased and reliable. A third round of interviews scheduled to begin in 2005 will collect additional information on agricultural exposures and health outcomes. The study can provide data to address many health issues in the agricultural community. The study investigators welcome collaboration with interested scientists.*

Keywords. *Agriculture, Cancer, Farmers, Injuries, Mortality, Pesticides, Prospective study, Respiratory disease.*

The Agricultural Health Study (AHS) was initiated because of an unique pattern of disease among farmers. Compared to the general population, farmers have a remarkable deficit in total mortality, total cancer, heart disease, lung cancer, and a number of other major causes of death that may be due to a low prevalence of tobacco and alcohol use and higher levels of physical activity (Blair et al., 1992). However, excess

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mortality has been reported for accidents, a few cancers (lip, stomach, skin, prostate, brain, soft-tissue sarcoma and leukemia, lymphoma, and multiple myeloma), non-malignant respiratory conditions, and some neurologic conditions (Cordes and Rea, 1991). Limitations of many previous investigations included use of data collected for administrative purposes, i.e., death certificates, census records, and tumor registries, with limited detail on specific agricultural exposures, or inability to adequately control for potential confounding. To more fully evaluate disease patterns in agricultural populations and to identify lifestyle, occupational, and environmental factors associated with various health outcomes, the National Cancer Institute (NCI), the National Institute of Environmental Health Sciences (NIEHS), and the U.S. Environmental Protection Agency (EPA) in 1993 launched a prospective cohort study of farmers, farmer's spouses, and commercial pesticide applicators in Iowa and North Carolina to serve as a research laboratory to monitor health issues in the agricultural population (Alavanja et al., 1999). The prospective nature of this study provides the opportunity to periodically obtain additional information on exposures and outcomes. A number of papers from the Agricultural Health Study have already appeared in the literature (Tarone et al., 1997; Coble et al., 2002; Dosemeci et al., 2002; Blair et al., 2002; Alavanja et al., 1998; Sprince et al., 2003; Kamel et al., 2000; Hoppin et al., 2002; Hoppin et al., 2003; Alavanja et al., 2003; Lee et al., 2004; Rusiecki et al., 2004; Flower et al., 2004; Alavanja et al., 2004). This article describes the cohort and provides a summary of findings to date.

Methods

The Agricultural Health Study, a prospective agricultural cohort in Iowa and North Carolina, is composed of 57,311 licensed pesticide applicators, including 52,395 private applicators (who are mostly farmers) and 4,916 commercial applicators (in Iowa only), and 32,347 spouses of private applicators for a total of 89,658 individuals (Alavanja et al., 1999, and in press). Participation was quite high among applicators (nearly 80%) (Tarone et al., 1997). The licensed applicators are mostly men (97%) and the spouses are mostly women (99%). Applicators enrolled in the AHS at county pesticide licensing facilities by completing a 21-page enrollment questionnaire. A state-issued license is required for the purchase of restricted-use pesticides in agriculture. Participants took home a second questionnaire to provide additional information on lifestyle factors, agricultural activities, and medical conditions. Only about 50% of the enrolled private applicators completed the take-home questionnaire (Tarone et al., 1997). Spouses of private applicators were also asked to enroll using two self-completed questionnaires.

Phase I (i.e., study recruitment) began in December 1993 and was completed in December 1997. The enrollment questionnaire sought information on crops, livestock, pesticides, and pesticide application methods, use of personal protective equipment, tobacco use, alcohol consumption, fruit and vegetable intake, medical conditions, diseases among first-degree relatives, physical activity, and basic demographic information. Phase I take-home questionnaires for applicators sought more detailed information on some pesticides, personal protective equipment use, various agricultural practices and tasks, dietary and cooking practices, and other occupational exposures. Spouses were asked to complete take-home questionnaires to provide basic demographic and lifestyle information, information on pesticide use, occupations outside the home, alcohol and tobacco use, drinking water source, pesticide use in the home, dietary and cooking practices, medical history, reproductive history, and information about their children. See the AHS website (www.aghealth.org) for more information about the study and details on collaborative procedures.

During Phase II (1998 through 2003), cohort participants were re-contacted and administered a computer-assisted telephone interview, given a self-completed mail dietary questionnaire, and asked to provide a buccal cell sample. The interviews sought information on pesticide use, other agricultural exposures, medical conditions, and lifestyle factors occurring since 1998, i.e., the completion of Phase I. Also during Phase II, comprehensive environmental and biologic monitoring visits were conducted on 84 farms by the U.S. EPA to provide quantitative information on pesticide exposures and to assess the validity of exposure estimates based on interview information. The National Institute for Occupational Safety and Health conducted monitoring studies to evaluate pesticide exposures among children and among orchardists. Phase III activities are being planned and will begin in 2005 to update information on agricultural exposures, lifestyle factors, and selected diseases and collect additional biologic specimens.

Deaths among cohort members are identified annually through the National Death Index (NDI) and state mortality files. Cancer incidence is determined by annual linkage of the cohort to the tumor registries in Iowa and North Carolina.

Results

Demographich Characteristics and Agricultural Exposures

Although mean follow-up of the cohort is less than 10 years, we have published a number of articles characterizing the cohort on methodological issues, on exposure assessment, and on cancer and other disease outcomes. Selected occupational and lifestyle characteristics of the cohort are shown in table 1. Forty-three percent of the farmers and 26% of the spouses reported ever using cigarettes, which is only about two-thirds the ever smoking rate for the remainder of the population. A wide range of farming operations was reported. North Carolina has a much more varied agriculture than Iowa; however, corn was the most common crop in both states (69%).

Nearly all men reported applying pesticides (94%), as did over half of the women (54%) (Alavanja et al., 1999). Most women applying pesticides were not licensed applicators. 2,4-D was the most common pesticide used by Iowa farmers, while glyphosate was more frequently used by North Carolina farmers and Iowa commercial applicators. The median number of days per year of pesticide application was 17 for Iowa

Table 1. Demographic and exposure characteristics of the Agricultural Health Study cohort at enrollment.

Factor		Farmers	Farmer's Spouses
State:	Iowa	31,853	21,771
	North Carolina	20,366	10,576
Gender:	Men	50,878	220
	Women	1,341	32,347
Age:	<50 years	29,697	18,632
	50+ years	22,506	13,715
13+ years education		43,110	28,947
Ever smoked		43%	26%
Applied pesticides:	Alachlor	48%	4%
	2,4-D	69%	14%
	Chlorpyrifos	39%	4%
	Diazinon	35%	10%
	Terbufos	35%	3%
Use pesticides in home		13%	74%
Raised:	Beef cattle	36%	33%
	Hogs	31%	29%
	Corn	69%	22%

farmers, 26 for North Carolina farmers, and 45 for Iowa commercial applicators. In both Iowa and North Carolina, sizable proportions of private applicators reported engaging in painting (74% in Iowa; 47% in N.C.), welding (78% in Iowa; 43% in N.C.), repair of pesticide equipment (64% in Iowa; 49% in N.C.), and replacing brake linings (13% in Iowa; 18% in N.C.) that could result in contact with potentially hazardous substances. A majority of farmers reported holding nonfarm jobs (74% in Iowa; 57% in N.C.) with various exposures including pesticides (7% in Iowa; 7% in N.C.), engine exhausts (21% in Iowa; 20% in N.C.), solvents 16% in Iowa, 16% in N.C.), welding fumes 16% in Iowa; 16% in N.C.), and grain dust (10% in Iowa; 4% in N.C.) (Coble et al., 2002).

A critical requirement of high-quality epidemiologic studies of pesticides and chronic disease is the need for quantitative assessment of exposure. Studies to date have largely employed a qualitative approach. To fulfill this need for quantitative assessments, in the Agricultural Health Study we obtained information on specific pesticides used, frequency and duration of use, the use of personnel protective equipment (PPE), and unusual exposure occurrences by questionnaire. This information was combined with data from the monitoring literature on exposure levels associated with various application methods, handling practices, and PPE to create an intensity scale of cumulative exposure for use in the epidemiologic analyses (Dosemeci et al., 2002). Mean intensity scores for various pesticides varied by state, gender, and type of applicator. For example, the 2,4-D mean intensity score among licensed applicators was 6.0 for Iowa and 7.6 for North Carolina, 6.4 for both men and women applicators, 6.1 to 6.2 across four age groups, and 6.3 for farmers and 4.9 for commercial applicators. These cumulative intensity estimates are used in the results from analyses of prostate cancer and pesticide exposure and cancers among atrazine and alachlor users presented in this article. A monitoring project has recently been completed to assess the validity of these intensity scales by comparing them with monitoring data on 2,4-D and chlorpyrifos from a sample of farmers in the study, and results will be available shortly.

Methodologic Findings

Methodological studies have evaluated the reliability of reporting by study participants. Only about half of the farmers returned the take-home questionnaire, which sought more detailed information on personal habits and potential exposures. We compared responses from the enrollment questionnaire (which was available on all participants) to evaluate potential biases that might exist between respondents and non-respondents for the take-home questionnaire (Tarone et al., 1997). Few substantive differences were evident. Cohort members who completed the take-home questionnaire were slightly older than those who did not, but differences for important lifestyle or agricultural exposures did not appear meaningful. Because of a change in state procedures for licensing pesticide applicators in Iowa, we obtained repeat enrollment questionnaires completed about one year apart from 4,088 participants (Blair et al., 2002). Percent exact agreement and kappa values were quite high for important lifestyle and farm factors. Exact agreement was in the 80% range for pesticide application methods and reported use of specific pesticides. Reliability decreased as more detailed reporting was requested, i.e., for frequencies and amounts of substances used. Exact agreement for years and days per year of use of specific pesticides ranged from 50 to 75%. Exact agreement for number of cigarettes per day was 76%, for alcohol drinks per day 71%, vegetable servings per day 35%, and fruit servings per day 40%. Agreement did not vary by age or education of the subjects, nor the size of their farming operation.

Injuries and Accidents

Pesticide-related health care visits were reported less frequently by women (odds ratio (OR) = 0.68; 95% confidence interval (CI) = 0.46-0.99) and those with some college

(OR = 0.79; 95% CI = 0.66-0.91) (Alavanja et al., 1998). Elevated risks for a health care visit from pesticide exposure were observed for North Carolinians compared to Iowans (OR = 1.33; 95% CI = 1.17-1.52) and commercial versus private applicators (OR = 1.77; 95% CI = 1.52-2.06). Use of protective equipment did not reduce risks (OR = 1.10; 95% CI = 0.96-1.23), and frequency of application of insecticides (OR = 1.43; 95% CI = 1.26-1.63 for 70 or more applications), but not herbicides, increased risks.

Farmers are at high risk for injury (Cordes and Rea, 1991). A nested case-control study in the AHS cohort found that elevated risk of injury was associated with working more than 50 hours per week (OR = 1.65; 95% CI = 1.23-2.21), having large numbers of livestock (OR = 1.77; 95% CI = 1.24-2.51), possessing more than a high school education (OR=1.61; 95% CI = 1.21-2.12), regular medication use (OR = 1.44; 95% CI = 1.04-1.96), and wearing a hearing aid (OR = 2.36; 95% CI = 1.07-5.20) (Sprince et al., 2003).

Chronic Diseases

In addition to linking the cohort to the National Death Index and to state cancer registries, the take-home questionnaire completed by private applicators provided information on other diseases and conditions. After adjusting for potential lifestyle confounders, risk of retinal degeneration was associated with orchards in Iowa and North Carolina (Kamel et al., 2000). This association appeared to be due to use of pesticides. Evaluation by pesticide and pesticide class found associations with fungicides in Iowa (OR = 2.0; 95% CI = 1.1-3.6) and North Carolina (OR = 1.7; 95% CI = 1.1-2.8) and with carbamate insecticides (OR = 1.9; 95% CI = 1.2-3.0) and fumigants (OR = 1.7; 95% CI = 1.0-2.9) in Iowa. Although the numbers were not large, significant trends were observed between retinal degeneration and lifetime days of use of the following fungicides: benomyl, captan, chlorothalonil, maneb, and metalaxyl.

Farmers are known to be a high-risk group for various nonmalignant respiratory diseases (Cordes and Rea, 1991). Although associations with animals and dusts are well established, relatively few studies have evaluated the role of pesticides. Among the 20,468 farmers reporting, 3,838 reported the presence of respiratory wheeze (Hoppin et al., 2002). Odds ratios rose with number of days per year of pesticide use. Specific pesticides linked with reported wheeze included herbicides (alachlor, atrazine, cyanazine, EPTC), insecticides (chlorpyrifos, malathion, parathion, and permethrin), and the fungicide metalaxyl. Exposure-response trends were also noted between reported wheeze and total number of livestock, specifically for poultry and dairy cows (Hoppin et al., 2003).

Based on 281,859 person years at risk and 1,669 cancers among farmers, and 26,790 person years and 92 cancers among commercial applicators, the cancer incidence through December 2001 (an average follow-up of 5.5 years) was compared with that in the general population of the two states (Alavanja et al., in press). The overall cancer rate among the farmers was less than that among the general population (standardized incidence ratio (SIR) = 0.80; 95% CI = 0.76-0.84). Significant deficits occurred for cancers of the colon, rectum, pancreas, lung, and urinary system. SIRs greater than 1.0 occurred for multiple myeloma and cancers of the lip, gallbladder, ovary, prostate, and thyroid. Among commercial applicators, the overall cancer SIR was 1.01. Excesses occurred for cancers of the lip and prostate. Follow-up of the AHS cohort for an average of 3.7 years also found mortality rates for many causes lower than in the general population (Blair et al., in press). The all-causes standardized mortality ratio (SMR) for farmers and their spouses was about 0.5. Causes with low SMRs included cancers of the lung (SMR = 0.3), female genital organs (SMR = 0.4), and bladder (SMR = 0.6) and diabetes (SMR = 0.3), cardiovascular disease (SMR = 0.5), and chronic obstructive pulmonary disease (SMR = 0.2). Causes of death with slight elevations included cancers of the lip, gallbladder, eye, and thyroid gland. Stratification by presence of livestock, corn, farm size, and duration of handling pesticides did not fundamentally change these findings. The short follow-up and limited number of deaths in some categories make these estimates unstable.

Prostate cancer has been found to be elevated among farmers in a number of earlier studies (Blair et al., 1992) and in the SIR analyses of the AHS cohort (Alavanja et al., in press). A factor analysis of AHS data identified three pesticide grouping use patterns, i.e., herbicides; fumigants and fungicides used in North Carolina; and chlorinated pesticides (Samanic et al., 2004). We found an increased risk associated with the chlorinated pesticide group, but not with the others. An exposure-response relationship was observed with methyl bromide and an interesting, but inconsistent, pattern with captan (table 2) (Alavanja et al., 2003). An analysis of prostate-pesticide associations found a higher risk of prostate cancer among individuals with a family history of this cancer than among those lacking such a history. Specific pesticides showing an interaction were: butylate (interaction odds ratio (IOR) = 1.93; 95% CI = 1.19-3.11), chlorpyrifos (IOR = 1.65; 95% CI = 1.02-2.66), coumaphos (IOR = 2.58; 95% CI = 1.29-5.18), fonofos (IOR = 2.04; 95% CI = 1.21-3.44), and permethrin (animal use) (IOR = 2.31; 95% CI = 1.17-4.56).

We are currently evaluating subcohorts of farmers with exposure to selected pesticides. Relative risks by frequency of reported use of two herbicides (alachlor and atrazine) are shown in table 3. Elevated relative risks among 26,510 alachlor-exposed applicators were observed for leukemia and bladder cancer in some exposure intensity quartiles, but none were statistically significant (Lee et al., 2004). Over 36,000 applicators reported using atrazine. No exposure-response gradient was noted for any cancer among the farmers exposed to atrazine, including prostate (Rusiecki et al., 2004).

Discussion

The AHS cohort was assembled in the 1990s to serve as a national resource to study causes of various diseases in the rural population. Detailed information on lifestyle, medical, and agricultural factors is obtained periodically by interview. Buccal cells from about one-half of the population provide a source of DNA for evaluation of the role of genetic factors and gene-exposure interactions in the development of disease. A pesticide monitoring project on 84 farms provides quantitative information on pesticide exposures. The cohort is just now achieving sufficient maturity for fruitful analysis of many important diseases and outcomes.

There have already been a number of important and interesting findings. As would be predicted from the literature, farmers and their spouses are a healthy group. Overall mortality (Blair et al., in press) and overall cancer incidence (Alavanja et al., in press) are quite low compared to the general population. Undoubtedly this reflects the positive health habits practiced in most farming population, such as low smoking rates, moderate use of alcohol, and a more physically active lifestyle. Cancers sometimes noted as excessive among farmers, i.e., cancers of the stomach, skin, brain, and lymphatic and hematopoietic systems, were not elevated, although numbers are small at this stage of follow-up. An analysis of prostate cancer found that incidence rates were elevated among farmers and commercial applicators, particularly for those reporting use of organochlorine pesticides (Alavanja et al., 2003). A new finding was a fairly strong exposure-response relationship with frequency and intensity of use of the fumigant methyl bromide. Several pesticides, including butylate, chlorpyrifos, coumaphos, fonofos, permethrin, and phorate, showed stronger associations with prostate cancer among individuals with a first-degree relative with this cancer than those lacking a family history. These are new leads for a cancer with a poorly understood etiology. Further evaluation of prostate cancer will include re-analysis when additional cases have occurred and use of genotyping to

Table 2. Relative risk of prostate cancer among applicators by cumulative exposure score category to selected pesticides.

	Cumulative Exposure Score Based on the Enrollment Questionnaire						
Pesticide	Un-exposed	1 Lowest	2	3	4	5 Highest	P for Trend
Alachlor							
OR		0.91	1.11	1.35	0.70	0.77	
(95% CI)	1.0	(0.70-1.18)	(0.85-1.45)	(0.95-1.92)	(0.44-1.12)	(0.48-1.26)	0.52
No. cases	303	81	82	40	20	20	
Atrazine							
OR		1.02	0.91	0.89	0.82	0.97	
(95% CI)	1.0	(0.79-1.31)	(0.71-1.18)	(0.65-1.23)	(0.54-1.25)	(0.63-1.48)	0.34
No. cases	202	113	114	57	27	28	
Carbofuran							
OR		1.29	1.93	1.00	0.68	1.01	
(95% CI)	1.0	(0.95-1.74)	(1.42-2.62)	(0.66-.51)	(0.38-.23)	(0.58-1.77)	0.23
No. cases	400	54	50	26	12	13	
Chlorpyrifos							
OR		0.95	1.04	0.89	0.64	0.73	
(95% CI)	1.0	(0.70-1.30)	(0.75-1.42)	(0.54-2.25)	(0.35-1.18)	(0.41-1.31)	0.23
No. cases	392	49	48	24	12	12	
Permethrin							
OR		1.30	2.31	1.11	1.73	0.74	
(95% CI)	1.0	(0.76-2.24)	(1.38-3.87)	(0.54-2.25)	(0.63-4.75)	(0.24-2.33)	0.63
No. cases	518	16	16	8	4	4	
Aldrin							
OR		1.44	1.12	1.56	0.87	1.38	
(95% CI)	1.0	(0.98-2.11)	(0.76-1.66)	(0.92-2.64)	(0.38-1.99)	(0.60-3.19)	0.70
No. cases	226	33	34	17	7	8	
DDT							
OR		1.18	1.17	0.76	1.38	1.14	
(95% CI)	1.0	(0.84-1.66)	(0.81-1.69)	(0.46-1.27)	(0.71-2.66)	(0.59-2.21)	0.89
No. cases	178	50	45	23	11	11	
Heptachlor							
OR		1.08	0.86	1.00	0.64	0.66	
(95% CI)	1.0	(0.67-1.74)	(0.53-1.41)	(0.51-1.98)	(0.20-2.03)	(0.21-2.09)	0.41
No. cases	273	20	19	10	6	3	
Methyl bromide							
OR		1.01	0.76	0.70	2.73	3.47	
(95% CI)	1.0	(0.66-1.56)	(0.47-1.25)	(0.38-1.28)	(1.18-6.33)	(1.37-8.76)	0.004
No. cases	482	23	22	11	6	5	
Captan							
OR		1.07	1.09	1.89	0.95	2.79	
(95% CI)	1.0	(0.50-2.30)	(0.48-2.48)	(0.58-6.12)	(0.23-3.93)	(0.35-22.1)	0.11
No. cases	518	7	6	3	2	1	

Table 3. Relative risk for selected cancers by cumulative exposure scores for alachlor and atrazine.

Cancer and	Alachlor		Atrazine	
Exposure Quartiles	No. Cases	OR (95% CI)	No. Cases	OR (95% CI)
All cancer				
1 - Lowest	189	1.0	340	1.0
2	188	1.37 (1.09-1.74)	338	0.97 (0.80-1.18)
3	188	1.42 (1.11-1.82)	338	0.96 (0.79-1.19)
4 - Highest	189	1.11 (0.84-1.46)	339	0.88 (0.71-1.11)
P for trend		0.39		0.28
Leukemia				
1 - Lowest	7	1.0	7	1.0
2	7	0.99 (0.27-3.58)	7	1.64 (0.63-4.25)
3	3	0.85 (0.19-3.73)	16	0.41 (0.11-1.49)
4 - Highest	9	2.83 (0.74-10.9)	11	0.56 (0.17-1.86)
P for trend		0.17		0.11
Multiple myeloma				
1 - Lowest	3	1.0	6	1.0
2	2	2.22 (0.29-16.9)	2	0.71 (0.12-4.30)
3	1	1.12 (0.09-14.4)	7	1.85 (0.42-8.24)
4 - Highest	5	5.66 (0.70-45.7)	8	2.17 (0.45-10.3)
P for trend		0.13		0.21
Non-Hodgkin's lymphoma				
1 - Lowest	5	1.0	17	1.0
2	3	0.62 (0.11-3.44)	16	0.88 (0.35-2.27)
3	10	2.40 (0.65-8.82)	15	1.36 (0.56-3.28)
4 - Highest	9	1.40 (0.32-6.11)	20	1.75 (0.73-4.20)
P for trend		0.42		0.14
Bladder				
1 - Lowest	4	1.0	10	1.0
2	8	3.11 (0.79-12.3)	14	1.21 (0.39-3.73)
3	10	3.64 (0.89-14.8)	12	1.01 (0.31-3.29)
4 - Highest	7	2.03 (0.41-10.0)	11	0.85 (0.24-2.94)
P for trend		0.44		0.71
Colon				
1 - Lowest	14	1.0	30	1.0
2	12	1.36 (0.56-3.34)	24	0.65 (0.33-1.28)
3	16	1.85 (0.76-4.50)	21	0.61 (0.30-1.25)
4 - Highest	17	1.14 (0.40-3.23)	33	0.86 (0.43-1.73)
P for trend		0.64		0.64
Prostate				
1 - Lowest	78	1.0	143	1.0
2	80	1.26 (0.88-1.78)	143	1.03 (0.76-1.41)
3	80	1.20 (0.82-1.74)	132	0.86 (0.62-1.20)
4 - Highest	63	0.74 (0.48-1.15)	134	0.89 (0.63-1.25)
P for trend		0.26		0.35

identify genetic polymorphisms that might contribute to the susceptibility findings. The pesticide-specific cohort analysis is a strong tool to assess the potential cancer risks associated with specific pesticide use. The associations between alachlor, leukemia, and bladder cancer are new leads, but require further assessment (Lee et al., 2004). Findings from analysis of exposure to atrazine provide little evidence of an increased risk at exposure levels experienced by farmers (Rusiecki et al., 2004).

The cohort has also provided important findings in the area of accidents, injuries, and nonmalignant diseases. Retinal degeneration has been found in dogs and rodents treated with pesticides, but epidemiologic data are scarce. The association with orchards and fungicides is a new lead (Kamel et al., 2000). Respiratory symptoms among farmers (Cordes and Rea, 1991) are well known to be associated with livestock and dusts (Hoppin et al., 2002), but the link with pesticides is less conclusive (Hoppin et al., 2002). Assessment of health care visits because of pesticide exposure (Alavanja et al., 1998) and agriculture-related injuries (Sprince et al., 2003) have provided new leads for improving the health of agricultural populations. The major factor relating to high pesticide exposure events, i.e., total lifetime pesticide application days, indicates that it may not be possible to design any single intervention to reduce these occurrences (Alavanja et al., 1998). The explanation for the associations between wearing a hearing aid and regular use of medications and risk of agricultural injury are unclear, but suggests that special efforts are needed to reduce risks for these two subgroups (Sprince et al., 2003).

Strengths of the Agricultural Health Study include its large size, the collection of exposure information prior to the development of disease, the detailed information on pesticide use practices and procedures for specific chemicals, the availability of information on agriculture and non-agriculture exposures, detailed information on potential confounding factors for most chronic diseases, and highly complete follow-up for mortality and cancer incidence. Methodologic studies have demonstrated that there is little evidence of bias from incomplete participation in various subcomponents of the study (Tarone et al., 1997) and that the reliability of reporting for pesticide use is adequate for sound epidemiologic studies (Blair et al., 2002). Furthermore, confounding from multiple exposures is unlikely to have much of an impact on relative risks (Tarone et al., 1997).

Current activities will focus on analyses of colon and breast cancer for occupational and lifestyle factors; cancer risks among additional pesticide-specific subgroups (i.e., chlorpyrifos and 2,4-D); extended analyses of prostate cancer risk and gene-pesticide exposure interactions; assessment of agricultural risk factors for neurologic, respiratory, and urinary tract nonmalignant diseases; agricultural exposures and risk of depression and rheumatoid arthritis; and nested studies of Parkinson's disease, immunologic abnormalities, and childhood cancer.

The funding agencies (NCI, NIEHS, and EPA) and their collaboration contractors (University of Iowa, Battelle, Inc., and Westat, Inc.) welcome collaboration and encourage interested investigators to review the Agricultural Health Study website (www.aghealth.org) and contact study investigators with research ideas.

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